weight of ethanol; (b) from about 10% to 60% by weight glycol; and (c) water (in original) in a volume percentage adding up to 100% by volume.

7. (twice amended) A process for the preparation of the solution according to claim 2, comprising [the steps of] dissolving the Tamoxifen Citrate in a mixture of the ethanol and glycol components, and then adding the water component and any other [components] ~~conventional~~ additives.

10. (amended) A pharmaceutical preparation according to claim 2, wherein the water component (c) contains additive(s) selected from the group consisting of flavors, sweeteners, and coloring agents.

11. (amended) A process according to claim 9, wherein the water component contains additive(s) selected from the group consisting of flavors, sweeteners and coloring agents.

add c3 =>

REMARKS

Claim 1, 2, 7, 10 and 11 are amended hereby. Claims 1 - 11 are still pending.

The claims have been amended to overcome the indefiniteness rejection. This rejection is now deemed moot. It is clear from the specification and the claims that the present invention is directed to a pharmaceutical solution of Tamoxifen Citrate for oral intake. This is the first disclosure of such a pharmaceutical solution, which was a long-sought pharmaceutical form with considerable advantages.

In the Office Action, the Examiner rejected claim 1 under §112, first paragraph, for undue breadth. This rejection is respectfully traversed.

The Examiner asserts that the specification does not enable the preparation of a solution in *any* solvent or mixture of solvents. A sufficiently concentrated pharmaceutical solution of

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Tamoxifen Citrate suitable for oral intake is a breakthrough with considerable advantages. As such, Applicants should be allowed reasonable scope in claiming their invention. The claimed invention is not directed to *any* solution, but one in which the solvent is usable in oral dosage form. How to make such a pharmaceutical solution in a suitable solvent is described in detail and exemplified (page 6), which makes clear to one skilled in the art what should and should not be done in order to carry out the invention. The skilled person has, therefore, an unambiguous direction to realize a product according to the invention. To restrict Applicants claim 1 any further is deemed unreasonable, because the feature "solution" is unambiguous and this is the first time a pharmaceutical solution for oral intake is found with this compound without chemical modification by the addition complexing agents (see specification page 2, line 7).

It is respectfully submitted that if each of the factors cited in *Ex parte Forman* is analyzed, a court would ultimately agree that it would not constitute undue experimentation to practice the invention claimed in claim 1. That Applicants had obstacles in obtaining the present invention should not have a negative impact on the scope of their claim.

Accordingly, this rejection should be reconsidered and withdrawn.

Claim 1 was rejected under §103(a) over WO '757 in view of Kraus. This rejection is respectfully traversed.

As pointed out in the present specification, solutions aided with complexing agents are not within the definition of "dissolved Tamoxifen" (see specification page 2, line 6 and 7, "without chemically altering it"). It is therein defined that the addition of complexing agents is considered a chemical modification of Tamoxifen. Such addition leads therefore not to a solution of Tamoxifen, but to a solution of the complex Tamoxifen-complexing agent. This distinction is made clear in the above amendment to claim 1. Clearly the present invention is not obvious based on a document (WO '757) that states that it is

a problem to dissolve Tamoxifen and resorts to complexing agents to solve the problem, in combination with another document (Kraus) in which no other method of dissolving Tamoxifen Citrate is disclosed. Therefore, reconsideration and withdrawal of this rejection are deemed proper.

Finally, claim 1 is rejected under §103(a) over WO '506. This rejection is also respectfully traversed.

WO '506 discloses a solution of Tamoxifen in N-methylformamide (NMF), which is indicated by listing Tamoxifen as one of the anti-tumor drugs that can be fused in NMF solutions or suspensions. WO '506 concerns the preparation of solutions for parenteral administration (page 1, line 12). NMF is not an acceptable solvent for an oral preparation, because it is a recognized teratogen and is toxic to the liver and lungs (see Rowinsky, E.K. et al., Clinical Pharmacology of Oral and IV N-methylformamide; pharmacological basis for lack of clinical anti-neoplastic activity. J. NAT Cancer Institute, 80:pp 671-678, 1988). Regulations state that any non-compendia material used in a pharmaceutical formulation must be supported with toxicological data. The solution of the present invention is for oral administration. One skilled in the art looking for a oral liquid preparation would not have consulted the document dealing with NMF. According, there is no motivation to derive the present invention from the disclosure of WO '506. This rejection should be reconsidered and withdrawn.

Applicants gratefully acknowledge the Examiner's indication that claims 2 - 11 are allowable. It is respectfully submitted, however, that all of claims 1 - 11 are allowable.

If the Examiner believes there are any minor issues remaining that could be resolved by a telephone conference, he is invited to contact the undersigned at the number listed below.

In the event this paper is not considered to be timely filed, Applicants hereby petition for the appropriate extension of time. Any fees for such an extension, along with any other

fees due in this application may be charged to our Deposit Account No. 02-2334.

Respectfully submitted,

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